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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,624	04/03/2001	Lorraine D. Butlin	IMIN.P-033	8891

21121 7590 06/13/2003

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 06/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/828,624	Applicant(s) Butlin et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 26, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *15-35* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *15 and 16* is/are allowed.

6) ☒ Claim(s) *18-35* is/are rejected.

7) ☒ Claim(s) *17* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-14 have been canceled.

Claims 17 and new claims 18-35 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

2. Claims 15-16 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Rejections/Objections Maintained

3. Claim 17 objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim must not depend from another multiple dependent claim, and depend from a prior claim in the alternative and not depend from multiple claims simultaneously. See MPEP § 608.01(n). Accordingly, the claim 17 will not been further treated on the merits.

Rejections Withdrawn

4. Claims 1-4,10-16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the cancellation of claims 1-4, 1-14, and Applicant's discussion of the meaning of the claim limitations set forth in claims 15-16.

5. Claim 1 rejected under 35 U.S.C. 102(b) as being anticipated by Hashimoto et al (1998), in light claim 1 having been canceled, and the claims are directed to the analysis of samples for gonadotropins, and not any analyte the exists in different forms.

6. Claims 1-4, and 13-14 rejected under 35 U.S.C. 102(b) as being anticipated by Rafferty, B et al (Journal of Endocrinology, 1995), in light of the fact that Rafferty et al analyze pooled samples, rather than a sample from an individual human female.

7. Claims 1-4, 13 and 14 rejected under 35 U.S.C. 102(b) as being anticipated by Chappel (US Pat. 5,262,518), in light of the claims having been canceled.

8. Claims 1-3, 13 rejected under 35 U.S.C. 102(b) as being anticipated by Evans, LW et al (May 1997), in light of the claims having been amended to recite the term "gonadotropin" and the analyte of Evans et al is not a gonadotropin molecule.

9. Claims 10, 12, 13 rejected under 35 U.S.C. 102(b) as being anticipated by May et al (WO88/08534), in light of the claims having been canceled and newly submitted claims reciting a different combination of claim limitations directed to two signal producing means for a gonadotropin.

10. Claims 10-14 rejected under 35 U.S.C. 102(e) as being anticipated by Magginetti et al (US Pat. 6,087,184), in light of the claims having been canceled and newly submitted claims reciting a different combination of claim limitations directed to two signal producing means for a gonadotropin.

11. Claims 10-11, 13 rejected under 35 U.S.C. 102(b) as being anticipated by Meyerhoff et al (US Pat. 5,830,680) in light of the claims having been canceled and newly submitted claims reciting a different combination of claim limitations directed to two signal producing means for a gonadotropin.

Response to Arguments

12. The objection to claim 17 was not traversed. The objection is maintained for reasons of record.

New Claims/New Claim Limitations/New Grounds of Rejection

Claim Objections

13. Claims 18 and 24 are objected to because of the following informalities

a. Claim 18 recites the step of "comprising the step of", but recites steps (a), (b) and (c); the word step should be --steps--.

b.Claim 24 should recite the plural of "assay" --assays-- as two different assays are repeated. Additionally, the word "is", is recited; it should be --the-- or --if the--. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

14. Claims 18-30, 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-30 are directed to the detection of two different forms of a gonadotropin in a human sample. What the different forms of the gonadotropin that correlates with and is indicative of the existence of a menopausal condition, especially when the individual is receiving hormone replacement therapy, the hormone of which has not been specifically defined not to be FSH, LH, GnRF, hCG or TSH, is not distinctly claimed. All forms of gonadotropom are not representative of a menopausal condition. What are the different forms being detected? The invention is not distinctly claimed.

Claims 18-22, 24-27 recite three methods steps: obtaining, performing and comparing. The performing step is not claimed as to perform the assay on the sample recited in the "obtaining" step. The rejection could be obviated by amending the claim to recite in paragraph (b), "performing contemporaneous first and second assays --on said sample--.

Claims 18-22, 24-27 are directed to a method for testing for a menopausal condition, but no correlation of the test results is determined from the comparing step. The first assay measures

a gonadotropin indicator that not does not correlate with any menopausal condition, and the second assay measures a second gonadotropin indicator. If the second assay produces a similar result to the first assay, paragraph (c), the "similar" result would not be indicative of a pre-menopausal, peri-menopausal or post menopausal condition. The first assay does not distinguish between pre-menopausal and post-menopausal conditions. A second assay producing similar result to the first assay would not provide means for distinguishing what condition exists relative to the first assay, as the first assay does not distinguish between pre-menopausal or post menopausal conditions. The invention is not distinctly claimed.

Claims 23 and 28 recite the phase "and the ratio of the two results is determined as an indication of menopausal status". Which number is in the numerator and which number is in the denominator? The first assay does not correlate with any type of menopausal status, and the second assay may or may not differ from the first assay when it produces a similar result. How can any ratio be an indication of menopausal status? An about 1/1 ratio would not indicate anything. The invention is not distinctly claimed, as any ratio would not be indicative of menopausal status, especially when the first assay does not correspond to any menopausal status. Clarification is requested.

Claim 31 recites in paragraph (c)the phrase: "means for combining the signals for the first and second gonadotropin responsive signal producing means", the preamble of claim 31 being directed to "An assay device". The cited phrase sets forth a combination of claim limitations that does not require the presence of the signal producing means from (a) and (b) to be part of the

device. The reagents in paragraphs (a) and (b) have differing functional characteristics and are not reactive/combinable one with the other, as they are directed to different indicators of a gonadotropin. The signal producing means from (a) and (b) are not required to be present in the claimed device, in light of the claim limitations requiring a combining means, and the combining means does not comprise the signal producing means from (a) and (b). The combination of claim limitations are unclear as no structural relation between each of the device components have been set forth in the claim, and the combining means recites a future tense phrase "means for combining", which does not require the presence of the signal producing means from (a) and (b) to be present in the device. Is the composition being claimed a kit? What is claimed does not define a device with inter-related components. Clarification is requested.

Claim 32 recites the phrase "signal indicative of follicle stimulating hormone". As follicle stimulating hormone is known to comprise cross reactive epitopes with other gonadotropins, how can any first and second gonadotropin-responsive signal producing means be indicative of follicle stimulating hormone when the signal could also be indicative of other gonadotropins if the reagents are not specific ? What "provided" means results in the recited indication? What reagent or reagents are a part of the claimed device?

Claims 33 and 35 recite the phrase "produce a signal as a result of binding in a detection zone". The device of claims 31 and 32, claims from which claims 33 and 35 depend, do not comprise a detection zone. No zones are recited in any claims from which claims 33 and 35

depend; the cited phrase lacks antecedent basis in the claims. No binding components have been so claimed to define a binding component for a zone.

Claims 33 and 35 recite the phrase " of a labeled specific binding reagent with a particulate direct label". Which of the two signal producing means comprises a particulate direct label? Does the device --further comprise-- an additional reagent? What is the specificity of the specific binding reagent that has not been provided in the claimed device? Is the labeled specific binding reagent an additional third labeling means? How many signal producing means are in the assay device? Clarification is requested.

Claim 34 depends from claim 32, and recites the phrase "wherein said labeled specific binding reagent is an antibody"; this phrase lacks antecedent basis in claims 31 and 32.

Claim Rejections - 35 U.S.C. § 102

15. Claims 18, 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Niccoli et al (1996, reference of record).

(independent claim 18) Niccoli et al disclose the claimed invention directed to a method of testing for a menopausal condition in a human, the method comprising the steps of

obtaining a gonadotropin-containing sample (lutropin containing sera, see page 747, coll. 1, lines 2) from a human female individual (woman and women, patient number for individuals) (see Niccoli et al page 745, Tab. 1);

performing contemporaneous first and second assays (12 different assays were performed, 1 assay using polyclonal antibodies which would measure total gonadotropin levels

(see Figure 2, page 742,legend; 11 assays that recognized at least 21 epitopes (see page 745, col. 2, middle of paragraph to end of column); additional assays used at least one anti-holomolecule (AB subunits present) monoclonal associated with an anti-beta subunit monoclonal (7/10) or an additional anti-AB subunit monoclonal (3/10); 1 kit used an anti-alpha subunit monoclonal antibody together with an anti-beta subunit monoclonal antibody (see page 746, narrative at top of page);

comparing the results of the first and second assays (see Tab. 1, page 745, bottom of page, column I or J (polyclonal, or other monoclonal assays) compared with all other assays using different combinations of monoclonal antibodies).

Instant claim 26: wherein the first and second assays are sandwich format (see page 746, which defines several sandwich formats for the first and second assays; page 747, col. 2).

Instant claim 27: different combinations of antibodies to the alpha and beta chains were used (see page 746, top of page)

16. Claims 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Matikainen et al (1992, reference of record).

(Claims 18, 19) Matikainen et al disclose the claimed invention directed to a method of testing for a menopausal condition in a human, the method comprising the steps of

obtaining a gonadotropin-containing sample (plasma from a human female individual (8 individuals were evaluated) (see pg. 820, col. 2, Subjects; page 821-page 822 : immunoradiometric assays; B-FSH and B-LH assay);

performing contemporaneous first and second assays (samples were taken every 10 minutes for 8 hours; bioactivity assay and immunoreactive assays; abstract and Figure 1, and Results section), the first assy being functional bioassay which determines biological activity independent of pre or pos t menopausal status and the second assay was an immunoassay using monoclonal antibodies (see abstract, first paragraph));

comparing the results of the first and second assays (see Figure 1, page 821, col. 2 and ratio determined from results, see page 822, Results section)

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

19. Birken et al (US Pat. 6,521,416): Birken et al disclose the claimed invention directed to a method of testing for a menopausal condition, the method comprising the steps of:

(a) obtaining a gonadotropin containing sample (urine, col. 29, line 61) from a human female individual (see col. 29, lines 4-7);

(b) performing contemporaneous first and second assays (sandwich assays: see col. 23, lines 18-41; two different forms of the gonadotropin:see col. 29, lines 45-57; the first assay was for hLH (total human LH) and the second assay was for hLH-beta-cf (fragment of LH associated with a menopausal condition);

(c) comparing the first and second assays (LH surges detected in the test were compared with levels of hLH-beta cf, see col. 29, lines 59-67 and col. 30, lines 1-17).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703)-308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
June 4, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,624	04/03/2001	Lorraine D. Butlin	IMIN.P-033	8891

21121 7590 09/20/2002

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	7

DATE MAILED: 09/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/828,624	Butlin et al
Examiner	**Art Unit**
Portner	1645

-- *The MAILING DATE of this communication appears n the cover sheet with the corresp ndence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event; however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 3, 2001*

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4 and 10-14* is/are rejected.

7) ☒ Claim(s) *5-9 and 15-17* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-17 are pending.

Allowable Subject Matter

1. Claims 15-16 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

3. Claims 5-9 and 17 are objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim must not depend from another multiple dependent claim, and depend from a prior claim in the alternative and not depend from multiple claims simultaneously. See MPEP § 608.01(n). Accordingly, the claims 5-9 and 17 have not been further treated on the merits.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4,10-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 1-4 are directed to methods, but no active voice methods steps are recited.

7. Claims 1-4, 13, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: providing a sample from a human female, conducting first and second assays, determining the level of gonadotrophin in each sample and comparing the results of first and second assays, determining the presence or absence of a menopausal condition.

8. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: providing a sample, providing reagents, and correlating the results with the preamble of the claim.

9. Claim 1 recites the phrases "plurality of forms" and "one form or the other". The preamble defines the presence or possibility of a plurality of forms while the body of the claim states that there are only two forms of the analyte. How many forms are being differentiated? How does comparing the results of the first and second assay differentiate the two states of the

analyte? Are both assays positive or negative? Clarification of what specifically provides for the assay to be able to differentiate between a plurality of forms.

10. Claim 10 recites the phrase "(preferably gonadotrophin-responsive)". In light of the phrase being set off by " ( )", are the limitations recited therein a part of the claim? Why are the limitations in brackets? What are the signal producing means? What is the specificity of the signal producing means? What is the reference standard in light of the fact that the analyte has not been defined? Is the reference standard a part of the device? What regents are included in the claimed device defined by functional language?

11. Claim 11 recites the phrase "wherein the gonadotrophin is FSH" and depends from claim 10. Claim 10 does not positively set forth claim limitations directed to "gonadotrophin", this term lacks antecedent basis in claim 10. This rejection could be obviated by amending claim 10 to positively set forth this term to provide antecedent basis.

12. Claim 13 recites the phrase "A method according to claim 1" "substantially as hereinbefore described". What is substantially the same? What is substantially different? How is claim 13 further limiting of the method of claim 1 without the recitation of a methods step? What does the method of claim 13 --further comprise--? The term "substantially" in claim 13 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. How this term

modifies the method of claim 1 to further limit the method, is not clearly set forth through the recitation of the relative term "substantially".

13. How is the device of claim 13 further limiting of the device of claim 10, if they are substantially the same? Or substantially different? Two different categories of invention, a device and a method, have been combined in claim 13 but are not interrelated to one another. Amendment of the claim to only recite a single invention is requested.

14. Claim 14 is a hybrid claim directed to a method and a device in the alternative. No method step is set forth to further limit claim 4. The phrase "first gonadotrophin-responsive signal producing means" lacks antecedent basis in claim 11. Claim 14 defines a use, and maybe intending to define a "Use" claim, a non-statutory category of invention. The phrase "as appropriate" is recited in claim 14. When is it appropriate? Are the reagents present in the device or not? Clarification of the claim is requested.

15. Claims 15-16 are unclear for the following reasons. Are the hybridomas that have been deposited been made publicly available, and all restrictions for public access been removed? Is the monoclonal antibody of claims 15-16 limited to the monoclonal antibody produced by hybridoma cell line ECACC 00032004, or ECACC 00032005, respectively? The claims appear to be claiming any monoclonal antibody to FSH, as long as it can be expressed. Is the claim language intended to define a genus of monoclonal antibodies or a species? How many <u>different</u> monoclonal antibodies are expressed by each deposit? Clarification is requested.

Claim Rejections - 35 U.S.C. § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

17. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Hashimoto et al (1998).

The claimed invention is directed to a method of differentiating between two states of an analyte that exists in a plurality of forms, the method comprising the steps of;

conducting two assays, the first being specific for one form and the second being reactive with all forms of the analyte; and

comparing the results form the first and second assays.

Hashimoto et al (1998) disclose a method of differentiating between two states of an analyte (20 kDa and 22 kDa of hCG) that exists in a plurality of forms, the method comprising the steps of;

For at least the following reasons, the Amendment After Final is not being entered:

1. The combination of the claim limitations of claim 18 and 29, results in a lack of clarity as to what sample is being analyzed at an interval of "at least one week" to further determine the menopausal statue of the female.

The definition of the term "contemporaneous" at page 8, lines 12-27 defines this term to include: Samples that have been sub-divided into multiple portions obtained from the same individual, or more than one sample obtained from the same individual on the same day, within a couple of hours of each other.

Claim 29 depends from claim 18(independent claim), and recites "further comprising the step of repeating the two contemporaneous assay after an interval of at least one week to determine is menopausal status of the human female individual is changing",

With the proposed amendment to recite "the same sample obtained from step a", claim 29 is unclear as to what sample is being analyzed that would meet the definition of contemporaneous samples. Claim 29 appears to be analyzing the "same sample" set forth in claim 18, but the sample of claim 18 that is "at least one week" old, would not meet the definition of "contemporaneous set forth in the instant specification.

The newly proposed combination of claim limitations set forth in claim 18 raises a new issue, as no changes could be determined on the same sample at least one week later, and a sample at least one week old does not meet the definition of a contemporaneous sample as defined in the instant specification.

2. Claim 31 (an assay device) is proposed to be amended to comprise "means for combining signals produced by the first and second gonadotropin-responsive signal producing means; changed from "means for combining the signals for the first and second gonadotropin-responsive signal producing means.

The currently pending claimed "means" reads on a bottle, test tube, assay device solid phase nitrocellulose strip; while the newly proposed claim limitations also reads on a light reading device that combines the signals to determine a level of emission which results in "combining the signals. The proposed claim limitations changes/modifies the scope of the claimed invention, and raises a new issue After Final.

3. Additionally, Claim 33 which currently recites the phrase "wherein the first and second gonadotropin-responsive signal producing means produce a signal" is proposed to recite "means" each "produce a signal", thus requiring two signal producing means, rather than "a signal" as currently recited in pending claim 33. The proposed claim limitations changes/modifies the scope of the claimed invention, and raises a new issue After Final.

4. Claim 34 is proposed to depend from claim 33, rather than claim 32, and would therefore recite a new combination of claim limitations not previously considered on the record for the claimed assay device.

5. Additionally, Claim 35 which currently recites the phrase "wherein the first and second gonadotropin-responsive signal producing means produce a signal" is proposed to recite "means" each "produce a signal", thus requiring two signal producing means,

rather than "a signal" as currently recited in pending claim 35. The proposed claim limitations changes/modifies the scope of the claimed invention, and raises a new issue After Final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

, Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April

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conducting two assays (see Figure 1, page 90, the first being specific for one form and the second being reactive with both forms, see mAb B13 reactive with both 20 kDa hCG and DO5 only reactive with the 20 kDa form; see section 3.2, page 81) the analyte; and

comparing the results form the first and second assays (comparison was based upon difference in determined optical density)

18. Claims 1-4, and 13-14 is rejected under 35 U.S.C. 102(b) as being anticipated by Rafferty, B et al (Journal of Endocrinology, 1995).

The claimed invention is directed to a method of differentiating between two states of an analyte that exists in a plurality of forms, the method comprising the steps of;

conducting two assays, the first being specific for one form and the second being reactive with all forms of the analyte; and

comparing the results form the first and second assays.

Rafferty, B et al disclose a method of differentiating between two states of an analyte (highly sialylated and less sialylated FSH) that exists in a plurality of forms, the method comprising the steps of;

conducting two assays (a sandwich assay with a reagent specific for the siaylated form of FSH and a sandwich assay for total FSH, relative to an international standard) the analyte; and

comparing the results form the first and second assays (comparison was based upon differences in sialylation relative to the international standard, see abstract).

19. Claims 1-4, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Chappel (US Pat. 5,262,518).

The claimed invention is directed to a method of differentiating FSH isoforms through carrying out at least two assays, to determine the presence or absence of menopause, through comparing the results from the first and second assays.

Chappel (US Pat. 5,262,518) disclose a method of differentiating FSH isoforms (see col. 2, lines 22-38)carrying out at least two assays, wherein the assays are based upon differences in the degree that FSH has been sialylated (see col. 2, lines 39-43), overall charge of the molecule, and metabolic clearance rate . The first assay is an isoelectric focusing assay of a sample to obtain a test result at PI value of greater than 5.5, to obtain a test result with a pI value of about 5.4 to 4.3 and to obtain a test result with a pI value of less than about 4.3, see col. 5, lines 13-24. The second assay follows the first through immunoaffinity column chromatography (see col. 5, lines 25-41).

Assay results are determine and compared for the presence or absence of isoforms based on charge, and the more heavily sialylated (more acidic) FSH present defines a sample from a post-menopausal woman (see col. 2, lines 39-45) being indicative of the presence or absence of menopause.

(Method of claims 13-14) Additionally the utilization of two monoclonal antibodies to detect total FSH is disclosed through Western blotting, with a monoclonal antibody specific for the alpha

subunit and a monoclonal antibody for the beta subunit (see col. 5, lines 42-46). The reference anticipates the instantly claimed invention.

20. Claims 1-3, 13 rejected under 35 U.S.C. 102(b) as being anticipated by Evans, LW et al (May 1997).

The claimed invention is directed to a method of differentiating two states of an analyte, the method comprising the steps of:

conducting two assays; and

comparing the results.

Evans, LW et al (May 1997) disclose to a method of differentiating two states of an analyte, the method comprising the steps of:

conducting two assays for activin isoforms, specifically activin A and activin-AB, the assay being a two-site enzyme-linked immunosorbent assay (see title), wherein a standard assay, and test sample were evaluated; and

comparing the results relative to the measure of total activin AB, the amount of activin-A in a pregnant women (pre-menopausal), and the amount in a postmenopausal serum sample for activin-A. The level of activin-A in a post-menopausal women were lower in serum than that found in a pre-menopausal woman. The reference anticipates the instantly claimed invention.

21. Claims 10-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Magginetti et al (US Pat. 6,087,184)

The claimed invention is directed to an assay device that comprises first and second analyte signal producing means, the first being constant irrespectively of the type of sample and the second providing a signal when the sample is derived from a pre-menopausal subject.

Magginetti et al disclose an assay device (see all figures) that comprises first and second analyte signal producing means (see claim 1), the first being constant irrespectively of the type of sample (see claims 10-11, 13) and the second providing a signal when the sample is derived from a pre-menopausal subject or post-menopausal subject (see claims 6, and 41-43 hCG, FSH, hPL). The signal generating means is a direct particle label (see claims 2-4 and claims 23-25). The device is formatted for a sandwich type immunoassay (see claim 8-9). The reference anticipates the instantly claimed invention.

22. Claims 10, 12, 13, are rejected under 35 U.S.C. 102(b) as being anticipated by May et al (WO88/08534.

The claimed invention is directed to an assay device that comprises first and second analyte signal producing means, the first being constant irrespectively of the type of sample and the second providing a signal when the sample is derived from a pre-menopausal subject.

May et al (WO88/08534) disclose an assay device (see all figures, page 3, lines 1-36) that comprises first and second analyte signal producing means (see page 5, lines 26-30), the first

being constant irrespectively of the type of sample (control zone that detects a control analyte, see page 9, lines 16-35) and the second providing a signal when the sample is derived from a pre-menopausal subject (see page 8, lines 1-10; pregnancy test for hCG, defines a pre-menopausal sample).

The reference also discloses a method of measuring different isoforms of a molecule, wherein one is glycated and the other is unglycated or the total concentration of the analyte is determined (see page 17,lines 20-23). An additional embodiment is the determination of two specific gonadotropins simultaneously (see page 17, lines 23-25).

The reference anticipates the instantly claimed invention.

23. Claims 10-11, 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Meyerhoff et al (US Pat. 5,830,680) .

The claimed invention is directed to an assay device that comprises first and second analyte signal producing means, one of which is FSH.

Meyerhoff et al disclose an assay device (see figures 1, 6-8) that comprises first and second signal producing means (see claims 6 and 8), one of which is an FSH specific reagent (see claim 6), the other being an analyte that is constant irrespective of menopause state, wherein the analyte is fibrinogen, hepatitis antigen or a viral protein (see claim 6 or 9) . The reference anticipates the instantly claimed invention.

Conclusion

24. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

25. Canfield et al (US Pat. 5,976,876) is cited to show a monoclonal antibody that is specific for hLHcf(core fragment) and is suggested to have the ability to distinguish between pre- and post-menopausal forms of the hormone.

26.Vlakirs (US Pat. 5,914,241) is cited to show an assay and kit for the determination of different forms of an analyte.

27. Birkern, S et al (1999); Burger, HG (1999); Vermes, I et al (1991); Matikainen, T et al (1992);Niccoli, P et al (1996); Zerfaoui et al (1996); Overlie, I et al (1999);Mellado, M et al (1996); Blethen, SL et al (1994); Boguszewski, et al (1996); Berger et al (1993); Canonne, C et al (1995); Kelly, JA et al (1997) ; Burger et al (1998); Jansson, C et al (1997); Hashimoto, Y et al (1998); Barth, JH et al (1997) are cited to show the existence of and/or methods of detecting different forms of the same analyte (abstracts only).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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September 16, 2002

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